

CORRECTED VERSION

(19) World Intellectual Property Organization
International Bureau(43) International Publication Date
20 October 2005 (20.10.2005)

PCT

(10) International Publication Number
WO 2005/097107 A2(51) International Patent Classification⁷: **A61K 31/404**,
31/437, 31/4188, 31/407, 31/5025, 31/5377, 31/496,
31/4439, 31/429, 31/4745, 45/06, A61P 35/00, C07D
209/34, 471/04, 487/04, 495/04, 491/04, 209/60, 209/30,
401/04, 513/04, 209/56, 409/04(21) International Application Number:
PCT/DK2005/000244

(22) International Filing Date: 8 April 2005 (08.04.2005)

(25) Filing Language: English

(26) Publication Language: English

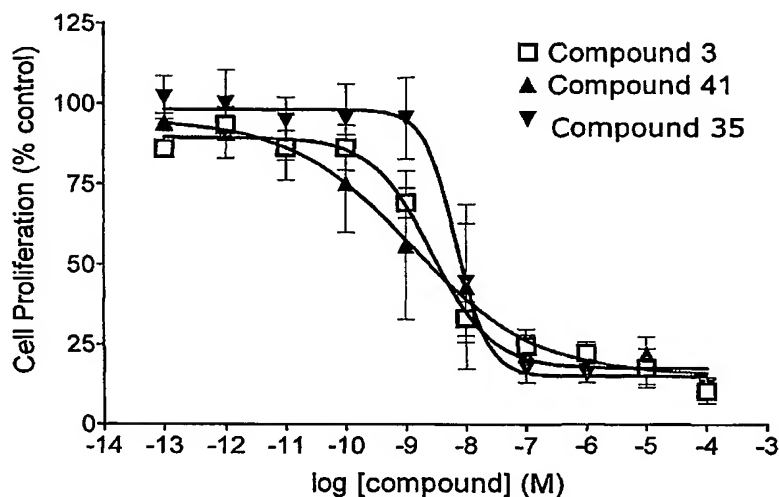
(30) Priority Data:
PA 2004 00576 8 April 2004 (08.04.2004) DK
PA 2004 00693 1 May 2004 (01.05.2004) DK
PA 2004 01153 27 July 2004 (27.07.2004) DK
PA 2004 01216 11 August 2004 (11.08.2004) DK(71) Applicant (for all designated States except US): **BIOIM-
AGE A/S** [DK/DK]; Mørkhøj Bygade 28, DK-2860
Søborg (DK).

(72) Inventors; and

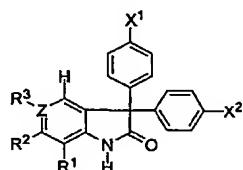
(75) Inventors/Applicants (for US only): **FELDING, Jakob**
[DK/DK]; Ordruphøjvej 29, 1, DK-2920 Charlottenlund
(DK). **PEDERSEN, Hans, Christian** [DK/DK]; Dan-
nevirkegade 6 st. tv, DK-1763 Copenhagen V (DK).
KROG-JENSEN, Christian [DK/DK]; Tværvej 3,
DK-2960 Rungsted Kyst (DK). **PRÆSTEGAARD,
Morten** [DK/DK]; Bueparken 130, DK-2750 Ballerup
(DK). **BUTCHER, Steven, Peter** [GB/DK]; Rothesgade
9, 1. th, DK-2100 Copenhagen (DK). **LINDE, Viggo**
[DK/DK]; J.E. Ohlsensgade 11, 3.th, DK-2100 Copen-
hagen (DK). **COULTER, Thomas, Stephen** [GB/GB];
Orchard Lodge, Grove Bridge, Wantage, Oxfordshire
OX12 7PA (GB). **MONTALBETTI, Christian** [CH/GB];
23 Reading Road, Wallingford, Oxfordshire OX9 9DS (GB).
UDDIN, Mohammed [GB/GB]; 18 Vale Road, Forest
Gate, London E7 8BJ (GB). **REIGNIER, Serge** [FR/GB];
78 Roebuck Court, Didcot, Oxfordshire OX11 8UU (GB).(74) Agent: **INSPICOS, A/S**; Bøge Allé 5, P.O. Box 45,
DK-2970 Hørsholm (DK).

[Continued on next page]

(54) Title: DIPHENYL OX-INDOL-2-ON COMPOUNDS AND THEIR USE IN THE TREATMENT OF CANCER



(57) Abstract: The present invention relates to substituted 3,3-diphenyl-1,3-dihydro-indol-2-one compounds, and the use of such compounds for the preparation of a medicament for the treatment of cancer in a mammal. It is postulated that treatment of cancers in which inhibition of protein synthesis and/or inhibition of activation of the mTOR pathway is an effective method for reducing cell growth. Examples of such cancers are breast cancer, renal cancer, multiple myeloma, leucemia, glia blastoma, rhabdomyosarcoma, prostate, soft tissue sarcoma, colorectal sarcoma, gastric carcinoma, head and neck squamous cell carcinoma, uterine, cervical, melanoma, lymphoma, and pancreatic cancer. A particular subclass of compounds are represented by the formula (II) wherein at least one of X¹ and X² is a heteroatom substituent, e.g. 6-chloro-3,3-bis-(4-hydroxy-phenyl)-7-methyl-1,3-dihydro-indol-2-one.



(II)



(81) **Designated States** (*unless otherwise indicated, for every kind of national protection available*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) **Designated States** (*unless otherwise indicated, for every kind of regional protection available*): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO,

SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— *without international search report and to be republished upon receipt of that report*

(48) Date of publication of this corrected version:

16 February 2006

(15) Information about Correction:

see PCT Gazette No. 07/2006 of 16 February 2006, Section II

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.